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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,411	01/08/2001	Franco Lori	NIH061.1CP1C2	5460

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EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,411	LORI ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/8/03 (Response)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

No claims have been cancelled, no claims have been amended, the disclosure has not been amended, and no new claims have been added as per the Response filed October 8, 2003. No additional Information Disclosure Statements or declarations have been filed as of the date of this Office action.

Claims **21-30** remain in the case.

Claims **21-30** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims **21-30** are directed to pairs of compounds, the specific chemical identities of which either have not been specified or have been only specified in part, and are therefore claimed more broadly than is supportable by the instant disclosed exemplification.

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant argues that *Regents of the University of California v. Eli Lilly* (119F.3d 1559 at 1568; 43 USPQ2d 1398 at 1406 (Fed. Cir 1997)) provides that "the written description for a claimed genus may ... be satisfied through sufficient description of a representative number of species by actual reduction to practice." Applicant further notes that the declaration of Dr. Vila supports the conclusion that the existence of a single successful embodiment (hydroxyurea + ddI) provides a sufficient basis for extrapolation to all of the combinations provided for by the instant claims. Examiner also notes the declaration filed April 7, 2003 by applicant's representative, Ms. Vensko, which states that Dr. Vila has a financial interest in the instant patent application. Applicant then cites various other prior art references which applicant alleges provide additional support for the extension of the single successful embodiment as part of the minimum supporting written description required for extrapolation to the entire generic class being claimed. Applicant also alleges that "[t]he phrases 'an inhibitor of ribonucleotide reductase' and 'an antiviral nucleoside phosphate analog' are as accurate as the subject matter permits, such components of a mixture being undefinable by 'chicken wire' structural formulas known to organic chemists."

Examiner respectfully disagrees. As a preliminary matter, applicant's comments about the limits of definition wherein the term "chicken wire" is found, are deemed to be directed to an issue under 35 U.S.C. §112, second paragraph, and will be dealt with in examiner's response following rejections under that portion of the statute. Examiner also notes that others have solved this problem using generic structural formulas; see many issued US patents in Class 514, subclasses 45-51.

To paraphrase a famous saying, the proof of the medical theory is in the testing. The theory looks promising, but as noted by Dr. Vila and his colleague Malley in US **5,521,161** (PTO-892 ref. **E**), the ddI/hydroxyurea combination only works in the treatment of HIV *in vitro* when ddI and hydroxyurea are administered in certain proportions and surprisingly Malley et al. admit that this combination does not work outside of this range. This highly unusual finding suggests the possibility that Malley and Vila's finding may be a singular observation not subject to extrapolation of the kind urged by applicant. Examiner looks forward to seeing test data in support of the asserted theory, but until such evidence is provided and found to be relevant and convincing, examiner remains skeptical and continues to believe that the instant written description is insufficient.

Extrapolation based on only a single data point is an impossible task when analyzing data plotable on a graph. The suggested extrapolation is similarly loaded with manifold possibilities for error. And, in conclusion, this debate is not effectively resolved in applicant's favor by Dr. Vila's declaration, partly because of the lack of supporting data therein, and partly because his personal interest in the instant application suggests that his declaration may be a self serving statement.

Claims **21-30** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in In re Wands (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims is difficult to determine because of reliance on functional terminology in claim **21** including the terms "an inhibitor of ribonucleotide reductase" and "an antiviral nucleoside phosphate analog."

B. The nature of the invention is limited to the inhibition of replication of a reverse transcriptase dependent virus in any host from a single cell to a complete human host. This encompasses the treatment of HIV in a human host.

C. The state of the prior art is well defined by the extensive list of prior art references in the PTO-892 and PTO-1449 of record. However, the prior art most relevant to the instant claims is limited to the patent and non-patent references from Mssrs. Malley and Vila (US 5,521,161 etc.) wherein the only operative embodiment supporting the instant claims is disclosed.

D. The level of one or ordinary skill is low because only a single prior art exemplification is known in the art.

E. The level of predictability in the art is low because of the existence of only a single enabling prior art exemplification (hydroxyurea/ddI) is known in the prior art.

F. The amount of direction provided by the inventor is, with the exception of the known exemplification, all prospective and therefore not useful in determining whether the prior art exemplification is a singular observation or whether analogous phenomena occur with other combinations of active ingredients.

G. The existence of working examples is limited to the single prior art exemplification, the remaining examples all being prospective; i.e. experimentally unsupported.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because of the absence of working examples to provide a proper basis for extrapolation to other combinations of active ingredients. See also *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991) which in its first opinion stands for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of

the efficacy of the alleged treatment (MPEP at 2107.03 (p. 2100-44, col. 2, in the August, 2001 revision)).

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

The above grounds of rejection has been amended to accommodate changes in PTO practice in the area of enablement rejections. While the form of the rejection is different, the substance of the rejection is unchanged.

Applicant argues, citing the Vila declaration, that the existence of a single working example (hydroxyurea/ddI) provides sufficient enabling support to permit the ordinary practitioner to select other combinations of active ingredients which applicant alleges will be both effective and synergistic if selected from the generic classes of claim **21**. Examiner respectfully disagrees and remains unconvinced in the absence of test data showing that extrapolation of the success of the Malley et al. **'161** patent (PTO-892 ref. **E**) may be realized in even a single additional combination. As well established in *Brenner v. Manson* (148 USPQ 689 (S. Ct. 1966), a patent is granted for an exploration already successfully completed, but is " ... not a hunting license."

Applicant needs to provide substantial additional guidance, preferably in the form of multiple test results. Such a showing would obviate the need for undue experimentation.

Claims **21-30** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims **21-30** one or both of the active ingredients have not been specified with other than with functional language, and therefore each noted claim lacks properly defined metes and bounds because the ordinary practitioner cannot determine what is included or excluded, or what was included or excluded at the time of filing.

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant argues at page 6 of the response that "[t]he phrases 'an inhibitor of ribonucleotide reductase' and 'an antiviral nucleoside phosphate analog' are as accurate as the subject matter permits, such components of a mixture being undefinable by 'chicken wire' structural formulas known to organic chemists." Examiner respectfully disagrees.

While applicant may not appreciate or readily comprehend the complexities of molecular structure represented by "chicken wire" formulas, this kind of representation is very well established as a means for defining chemical identities. Moreover, the terms initially found in claim **21** exemplify the reasons why functional terms defining active ingredients are inappropriate in medicinal method of treatment claims: they fail to provide the ordinary practitioner with an adequate basis for defining which particular compounds fit within the metes and bounds of the instant claimed subject matter and which compounds do not. If applicant has an alternative approach to solving this problem, examiner encourages the introduction of same at applicant's earliest convenience.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-30** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***12-22*** of U.S. Patent No. **6,046,175** (PTO-892 ref. **H**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-30** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***3-8*** of U.S. Patent No. **6,194,390** (PTO-892 ref. **J**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-28** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-3*** of U.S. Patent No. **5,521,161** (PTO-892 ref. **E**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-30** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-3*** of U.S. Patent No. **5,736,527** (PTO-892 ref. **G**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-30** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***6-8*** of U.S. Patent No. **6,093,702** (PTO-892 ref. **K**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

Applicant's arguments filed October 8, 2003 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. §1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number to send an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
03/16/2004

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600